



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,593	08/26/2003	Fci Huang	D0273 NP	5265
23914	7590	08/08/2007	EXAMINER	
LOUIS J. WILLE			SWOPE, SHERIDAN	
BRISTOL-MYERS SQUIBB COMPANY			ART UNIT	
PATENT DEPARTMENT			PAPER NUMBER	
P O BOX 4000			1652	
PRINCETON, NJ 08543-4000			MAIL DATE	
			08/08/2007	
			DELIVERY MODE	
			PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/648,593	Applicant(s) HUANG ET AL.	
	Examiner Sheridan L. Swope	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-51 is/are pending in the application.
- 4a) Of the above claim(s) 42-51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 August 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>0205;0507;0707;1006;1206</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' Request for Continuing Examination of May 16, 2007, in response to Final Rejection of this case mailed December 19, 2006, is acknowledged. It is acknowledged that applicants have amended Claim 41. Claims 41-51 are pending. Claims 42-51 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claim 41 is hereby considered.

Drawings-Objections

Figures 1 and 7 are objected to because they are not legible.

Figure 2 is objected to because the vertical line separating panels A & B is in the wrong place.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Provisional rejection of Claim 41 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 16 of US Application 11/072,175, for the reasons set forth in the prior action of March 14, 2006, is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1652

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

For Claim 41, the phrases “indicative of sensitivity” and “indicative of resistance” render the claim indefinite. It is unclear whether said “sensitivity” and “resistance” means the effect of the inhibitor on EphA2 expression or the effect of the drug to treat cancer cells. Furthermore, if the meaning is the effect of the drug to treat cancer cells, it is unclear whether the effect on cancer cells is cell death, reduction of growth rate, reduction of invasiveness, or some other parameter. The skilled artisan would not know the metes and bounds of the recited invention. For purposes of examination, it is assumed that sensitivity means the inhibitor reduces growth of the breast cancer cell, while resistance means the inhibitor does not reduce growth of the breast cancer cell.

For Claim 41, the phrases “increased expression of... [EphA2] ...is indicative of sensitivity” and “decreased expression of... [EphA2] ...is indicative of resistance” render the claim indefinite. The art clearly taught that EphA2 is increased in breast cancer cells and can cause tumorigenesis of mammary epithelial cells (Zelinski et al, 2001). In addition, it was known that reduction of EphA2 expression inhibits growth and invasiveness of breast cancer cells (Carles-Kinch et al, 2002). Thus, the skilled artisan would have known that a drug-induced reduction of EphA2 expression would indicate sensitivity of cancer cells to the drug, while failure to reduce EphA2 expression, or an increase in expression, would indicate resistance. For these reasons, the phrases “increased expression of... [EphA2] ...is indicative of sensitivity” and “decreased expression of... [EphA2] ...is indicative of resistance” render the claim indefinite.

Claim 41 recites a method wherein the effect of an inhibitor to increase or decrease expression of an EphA2 gene product is measured. However, the claim fails to define how the "increase" or "decrease" is assessed, i.e., what is compared. For example, the method might compare EphA2 expression with and without inhibitor or, alternatively, might compare the effect of inhibitor on EphA2 expression in cancer cells to expression in normal cells. The metes and bounds of the recited invention are unclear. Thus, Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. For purposes of examination, it is assumed that the recited method compares EphA2 expression in a cancer cell with and without inhibitor.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claim 41 is rejected under 35 U.S.C. 112, first paragraph/lack of enablement. The specification is enabling for determining in which of the eleven breast cancer cell lines of Figure 2A Upper the pleiotropic protein tyrosine kinase inhibitor BMS-A increases or decreases expression of an EphA2-encoding mRNA. However, the specification does not reasonably provide enablement for identifying the sensitivity of any breast cancer cell to any pleiotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the increased expression of an EphA2 gene product. Likewise, the specification does not reasonably provide enablement for identifying the resistance of any breast cancer cell to any said pleiotropic inhibitor by measuring the decreased expression of an EphA2 gene product. The

Art Unit: 1652

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claim 41 is so broad as to encompass a method for identifying the sensitivity of any breast cancer cell to any pleotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the increased expression of a EphA2 gene product. Claim 41 also encompasses a method for identifying the resistance of any breast cancer cell to any said pleotropic inhibitor by measuring the decreased expression of a EphA2 gene product. The scope this claim is not commensurate with the enablement provided by the disclosure with regard to correlating the effect of any said pleotropic inhibitor on inhibiting any cancer cell's growth, i.e. sensitivity, to increased expression of EphA2. Likewise, the claims's scope is not commensurate with the enablement provided by the disclosure with regard to

Art Unit: 1652

correlating the effect of any said pleotropic inhibitor on not inhibiting any cancer cell's growth, i.e. resistance, to decreased expression of EphA2.

The specific reagents and steps used determine the success of any diagnostic method. Predictability of which steps and reagents can be used to obtain the desired diagnosis requires a knowledge of, and guidance with regard to how said steps and reagents relate to the desired analysis. In the instant case, determining the sensitive of any breast cancer cell to any pleotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring expression of a EphA2 gene product requires the following. (1) That the EphA2 gene product serves as a marker in every cancer cell. (2) That Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and/or EphA2 regulate the expression of the EphA2 gene product in every cancer cell. (3) That inhibition of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and/or EphA2 is sufficient to regulate expression of the EphA2 gene product in every cancer cell. However, in this case the disclosure is limited to determining whether the protein tyrosine kinase inhibitor BMS-A enhances or inhibits expression of an EphA2-encoding mRNA in the eleven breast cancer cell lines of Figure 2AUpper.

It is acknowledged that methods for determining if EphA2 gene products are expressed in a cell are known in the art. However, if an EphA2 gene product is not expressed and cannot be used as a marker, the full scope of the recited invention cannot be practiced. It is also acknowledged that methods for determining whether a particular protein tyrosine kinase regulates the expression of a EphA2 gene product and whether inhibition of that particular kinase is sufficient for regulating expression of a EphA2 gene product are known in the art. However, it is not routine to screen the essentially unlimited number of breast cancer cells for a role for one

Art Unit: 1652

or more of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 in regulating the expression of an EphA2 gene product and whether inhibition of one or more of said kinases is sufficient to regulate the expression of an EphA2 gene product. Moreover, if such a role cannot be established, the full scope of the recited invention cannot be practiced. If a cancer cell does not respond to the tested inhibitor with an altered expression of an EphA2 gene product it may be because (1) the cell does not express EphA2, (2) Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and/or EphA2 do not regulate EphA2 gene product expression in the cell, and/or (3) inhibition of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and/or EphA2 is not sufficient to regulate EphA2 gene product expression in the cell, i.e., there is an additional pathway(s) for regulation of expression. Moreover, the art teaches away from increased expression of EphA2 being indicative of sensitivity of breast cancer cells to an inhibitor, as recited in the instant invention. For example, Zelinski et al teach that EphA2 is increased in breast cancer cells and can cause tumorigenesis of mammary epithelial cells (Zelinski et al, 2001), while Carles-Kinch et al teach that reduction of EphA2 expression inhibits growth and invasiveness of breast cancer cells (Carles-Kinch et al, 2002). Thus, the skilled artisan has little expectation that the recited invention can be used successfully.

The specification does not support the broad scope of Claim 41, which encompasses a method for identifying the sensitivity of any breast cancer cell to any pleiotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the expression of an EphA2 gene product. The specification does not support the broad scope of Claim 41 because the specification does not establish: (A) the identity of cancer cells for which an EphA2 gene product can serve as a marker; (B) the identity of cancer cells having a regulation

Art Unit: 1652

of EphA2 gene product expression by Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and/or EphA2; (C) whether inhibition of one or more of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 is sufficient to regulate EphA2 gene product expression; (D) the identity of any cancer cells wherein the effect of a pleiotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 to increase expression of an EphA2 gene product can be correlated to inhibition of cell growth; (E) the identity of any cancer cells wherein the effect of a pleiotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 to decrease expression of an EphA2 gene product can be correlated to lack of inhibition of cell growth; (E) a rational and predictable scheme for determining which cancer cells can be successfully analyzed with the recited method; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including identifying the sensitivity of any breast cancer cell to any pleiotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the increased expression of an EphA2 gene product and identifying the resistance of any breast cancer cell to any said pleiotropic inhibitor by measuring the decreased expression of an EphA2 gene product. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of cells having the desired biological characteristics allowing for successful analysis is unpredictable and the experimentation left to

Art Unit: 1652

those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

In support of their request that the prior rejection of Claim 41 under 35 U.S.C. 112, first paragraph lack of enablement, be withdrawn, Applicants provide the following arguments.

(A) Claim 41 has been amended to delete the phrase “one or more of the following”.

(B) BMS-A is an inhibitor of each one of the protein tyrosine kinases recite in Claim 41.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that Claim 41 has been amended to delete the phrase “one or more of the following”. It is also acknowledged that deletion of said phrase reduces the scope of the recited invention. However, for the reasons stated above, Claim 41 is rejected under 35 U.S.C. 112, first paragraph, because the full scope of the recited invention is not enabled by the specification.

(B) Reply: It is acknowledged that the specification teaches that BMS-A is an inhibitor of each one of the protein tyrosine kinases recite in Claim 41. However, said teaching does not enable the skilled artisan to make and use the full scope of the invention, identifying the sensitivity of any breast cancer cell to any pleotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the increased expression of a EphA2 gene product and identifying the resistance of any breast cancer cell to any said pleotropic inhibitor by measuring the decreased expression of a EphA2 gene product.

For these reasons and those explained in the prior action, Claim 41 is rejected under 35 U.S.C. 112, first paragraph/lack of enablement.

Written Description

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 41 is directed to a genus of methods wherein, upon treatment with any pleotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2, increased expression of EphA2 is indicative of sensitivity of breast cancer cells to the inhibitor, while decreased expression of EphA2 is indicative of resistance of breast cancer cells to the inhibitor. The specification fails to provide any example of sensitive cells wherein, increased expression of EphA2 is correlated to an effect of the inhibitor to reduce growth of the breast cancer cell. Likewise, the specification fails to provide any example of resistant cells wherein, decreased expression of EphA2 is correlated to an effect of the inhibitor to fail to decrease growth of the breast cancer cell. Given this lack of description of representative species encompassed by the genera of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In support of their request that the prior rejection of Claim 41 under 35 U.S.C. 112, first paragraph insufficient written description, be withdrawn, Applicants provide the following arguments.

(C) Claim 41 has been amended to delete the phrase "one or more of the following".

(D) BMS-A is an inhibitor of each one of the protein tyrosine kinases recite in Claim 41.

Art Unit: 1652

These arguments are not found to be persuasive for the following reasons.

(C) Reply: It is acknowledged that Claim 41 has been amended to delete the phrase "one or more of the following". It is also acknowledged that deletion of said phrase reduces the scope of the recited invention. However, for the reasons stated above, Claim 41 is rejected under 35 U.S.C. 112, first paragraph, because the full scope of the recited invention was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(D) Reply: It is acknowledged that the specification teaches that BMS-A is an inhibitor of each one of the protein tyrosine kinases recite in Claim 41. However, for the reasons explained above, said teaching does not describe the full scope of the invention, identifying the sensitivity or resistance of any breast cancer cell to any pleotropic inhibitor of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, BCR-ABL, PDGFR, c-Kit, and EphA2 by measuring the expression of a EphA2 gene product.

For these reasons and those explained in the prior action, Claim 41 is rejected under 35 U.S.C. 112, first paragraph/written description.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Examiner's note: In the interest of compact prosecution, this rejection is based on the assumption that, for the recited method, the effect of an inhibitor to decrease EphA2 expression in a cancer cell correlates with inhibition of the cancer cell's growth, i.e., sensitivity.

Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kassenbrock et al, 2002 in view of Wang et al, 2002 and further in view of Ogawa et al, 2000 or Zelinski et al, 2001. Kassenbrock et al teach that, in a human breast cancer cell line, the Src-class tyrosine kinase inhibitor PP1 inhibits Cbl phosphorylation (Fig 6) and EGF-R ubiquitination (Fig 8) leading to the proposal that phosphorylation of Cbl by a Src-class kinase leads to ubiquitination and down-regulation of the EGF-R (pg 24974; parg 8). Kassenbrock et al do not teach that PP1 regulates the expression level of EphA2. Wang et al teach that Cbl down-regulates EphA2 (Fig 2). Based on said teachings, a person of ordinary skill in the art would believe that, more likely than not, PP1 by inhibiting Cbl phosphorylation would also down-regulate EphA2. Both Ogawa et al (Table 1) and Zelinski et al (Fig 1) teach that EphA2 is highly expressed in breast cancer cells. Zelinski et al further teach that over expression of EphA2 causes malignant transformation of mammary epithelial cells (Fig 3 & 4). Thus, based on the combined teachings of Kassenbrock et al, Wang et al, Ogawa et al, and Zelinski et al the skilled artisan would believe that, more likely than not, down-regulation of EphA2 by PP1 would inhibit tumor growth and survival. It would have been obvious to a person of ordinary skill in the art to use the method of Kassenbrock et al to test the effect of PP1 on EphA2 expression levels in breast cancer cells and to conclude that, if EphA2 was down-regulated by PP1, the cancer cell growth would be inhibited by treatment with PP1. Motivation to use said methods derives from the desire to determine if PP1 would be successful for treatment of a patient with breast cancer. The

Art Unit: 1652

expectation of success is high, as high levels of EphA2 are predictive of tumor growth and the art teaches that, more likely than not, PP1, via inhibition of Cbl phosphorylation, would down-regulate EphA2. Therefore, Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kassenbrock et al, 2002 in view of Wang et al, 2002 and further in view of Ogawa et al, 2000.

In support of their request that the prior rejection of Claim 41 under 35 U.S.C. 103(a) as being unpatentable over Kassenbrock et al, 2002 in view of Wang et al, 2002 and further in view of Ogawa et al, 2000 be withdrawn, Applicants provide the following argument, which is relevant here. Claim 41 has been amended to delete the phrase "one or more of the following". PP1 is known to be only an inhibitor of Lck, Fyn, Zap-70, Jak2, and EGF-R. Accordingly, since PP1 is not known to inhibit the kinases specified in Claim 41, the Examiner's rejection of Claim 41 under 35 USC 103(a) is rendered moot.

This argument is not found to be persuasive for the following reasons. PP1 was originally identified as an inhibitor of Src family tyrosine kinases (Hanke et al, 1996), including Src, Fgr, Fyn, Yes, Blk, Hck, Lck, and Lyn. PP1 was also known to inhibit the PDGF-R (Waltenberger et al, 1999). More recently, PP1 has been demonstrated to also be an inhibitor of Kit and Bcr-Abl (Tatton et al, 2003). The specification states: "compounds that modulate, e.g., inhibit, protein tyrosine kinase or protein tyrosine kinase activity" are used to identify markers (pg 29, para 1). Thus, "inhibitor" encompasses compounds that reduce levels of EphA2 protein. As explained in the original rejection of Claim 41 under 35 U.S.C. 103(a), the combination Kassenbrock et al and Wang et al teaches that inhibition of Src inhibits EphA2 by inhibiting expression thereof. Thus, PP1 inhibits each of Src, Fgr, Fyn, Yes, Blk, Hck, Lck, Lyn, Bcr-Abl,

Art Unit: 1652

the PDGF-R, Kit, and EphA2. Therefore, Applicants' argument that PP1 is not known to inhibit the kinases specified in Claim 41 is not found to be persuasive.

For these reasons and those explained in the prior action, rejection of Claim 41 under 35 U.S.C. 103(a) as being unpatentable over Kassenbrock et al, 2002 in view of Wang et al, 2002 and further in view of Ogawa et al, 2000, is maintained.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Art Unit: 1652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943.

The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1652



SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER